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ORIGINAL ARTICLE

Screening for sickle trait among potential live kidney donors: policies and practices in US transplant centers

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Summary

Sickle cell trait is common in the United States (US) and associated with abnormalities of renal function. Little is known, however, about the potential risk of sickle cell trait to live kidney donors. Using an original questionnaire, we assessed the policies and practices of US renal transplant centers with regard to screening for sickle trait among potential live kidney donors. Fifty-four percent (137/252) of centers responded. Eighty-three percent (113/137) of transplant centers had no policy to screen donors for sickle trait. Thirty-four percent (46/135) of centers reported actually screening donors for sickle trait in practice. Thirty-seven percent (39/105) of centers reported excluding donors with sickle trait always or most of the time. High volume centers (>100 live donor transplants/year) were more likely to screen for sickle trait (Fisher's exact, $P = 0.03$), but not more likely to exclude potential donors with sickle trait from donating. Most US renal transplant centers do not screen donors for sickle trait. Wide variation is evident in center practice regarding exclusion of donors on the basis of sickle trait. Research into the potential impact of sickle trait on renal function after donation is needed to guide transplant clinicians.

Introduction

The practice of live donor kidney transplantation rests on the ethical foundation of minimizing the health risks of live kidney donors while facilitating transplantation for recipients [1,2]. As live donor kidney transplantation has become more common in the United States and elsewhere, the issue of whether to accept donors with isolated medical abnormalities has become more important [3,4]. Sickle cell trait is common in the United States (US) and associated with abnormalities of renal function [5]. Little is known, however, about the policies and practices of renal transplant centers towards live donors with sickle trait.

No policy has been articulated by major US transplant societies regarding screening for sickle trait among live donors, excluding donors on this basis, or addressing the possible risk of sickle trait with donors. The international forum of the Transplantation Society in Amsterdam did not address sickle trait [6]. The United Kingdom guidelines suggest testing for the trait 'where indicated' but do not discuss how to manage potential donors who test positive [7]. An expert review regarding live donors in the *American Journal of Kidney Disease* advocated further study of this issue [4].

Approximately 3 million Americans are estimated to have sickle trait, although many may be unaware [8]. Eight percent of black Americans have sickle trait and the trait is also common among patients with Mediterranean or Indian subcontinent heritage [9,10]. The prevalence of sickle trait among potential and actual kidney donors in the US remains unknown.

Renal abnormalities related to sickle trait range from isosthenuria, to hematuria, to the rare presentation with frank acute renal failure in the context of severe physical stress, such as military training [5,11]. The

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phenotype of disease depends on the patient's overall hemoglobin genotype and exposure to environmental stressors [5,12]. An increased incidence of medullary renal carcinoma has also been reported among sickle trait patients [13]. We are unaware, however, of studies that have examined the effects of sickle trait in the single-kidney state.

Using a questionnaire, we assessed the policies and practices of US kidney transplant centers with regard to sickle trait among kidney donors. We hypothesized that a minority (<50%) of transplant centers in the United States would have a policy or practice of screening donors for sickle trait, and that a small minority (<15%) would exclude donors with known sickle trait.

Patients and methods

We developed an original questionnaire to assess policies and practices at US transplant centers. The questionnaire can be found as Fig. 1.

The questionnaire addressed five domains related to the center. The first question elicited information about the presence of a policy to screen live kidney donors for sickle trait. The second asked about actual screening practices for sickle trait among donors and about which ethnic groups are screened. The third question asked about the frequency with which a sickle trait patient would be excluded from donation. The last one asked respondents to indicate the annual live donor kidney transplant volume at the transplant center.

The questionnaire was assessed for face and content validity among expert transplant clinicians, as well as general internists with expertise in questionnaire development, at the Brigham and Women's Hospital. Several revisions were made on the basis of feedback. We then piloted the questionnaire with ten transplant nephrologists known to the authors at different transplant centers located across the United States. No further revisions were made based on this pilot.

A list of US transplant centers was obtained from the United Network of Organ Sharing (UNOS). Mailing labels for the medical directors of these transplant centers were purchased from UNOS. Questionnaires were sent to all renal transplant centers in the US during 7/2005. We subsequently made at least two attempts over the phone to contact all renal transplant centers that had not responded to the mailed questionnaire. Follow-up questionnaires were sent to these centers by fax.

Statistical analyses were performed using the Stata 7.0 (Stata Corp, College Station, TX, USA). Comparisons between groups were made using chi square or Fisher's exact test, if the expected cell value was <5.

The study was exempted from review by the Brigham and Women's Institutional Review Board.

Results

Two hundred fifty-two renal transplant centers were contacted and 137 completed questionnaires (54% of total centers.) Results are displayed in Table 1. In the text

1) Does your transplant program have a policy about screening prospective living kidney donors for sickle cell trait? **Yes** **No**
If yes, please describe your policy:

2) Regardless of policy, do clinicians at your program screen prospective kidney donors for sickle cell trait? **Yes** **No**

a) If yes, which groups do you screen? (*please circle appropriate groups*)
Patients with suspected African heritage
Patients with suspected Mediterranean heritage
Patients with suspected Indian subcontinent heritage
All patients
Other _____

3) If a patient has sickle cell trait, would your program exclude that patient from donating a kidney? *(please circle one answer)*
Always **Most of the time** **Rarely** **Never**

4) Approximately how many living donor kidney transplants did your center do last year? *(please circle one answer)*
<50 **50 – 100** **>100**

Figure 1 Questionnaire.

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Table 1. Questionnaire results.

Question and response	Number (%)
Question 1: Center policy toward screening for sickle trait (n = 137)	
No	113 (82.5)
Yes	24 (17.5)
Question 2: Center practice toward screening for sickle trait (n = 135)	
No	89 (65.9)
Yes	46 (34.1)
Question 2a: Which groups are screened (n = 46)	
Patients with suspected African heritage	19 (40.4)
Patients with suspected African heritage & patients with suspected Mediterranean heritage	8 (17.4)
Patients with suspected African, Mediterranean or Indian heritage	6 (13.0)
All patients	3 (6.5)
Other	10 (21.7)
Question 3: Center practice toward excluding donors with sickle trait (n = 105)	
Exclude always	19 (18.1)
Exclude most of the time	20 (19.1)
Exclude rarely	49 (46.7)
Exclude never	17 (16.2)

below, percentages correspond to the proportion of centers responding to that question.

Only 24 centers (18%) reported having a policy regarding screening for sickle trait (question 1). A blank space was provided for respondents with a policy to describe the policy. Fifteen centers described a policy to screen patients with a family history of sickle cell disease. Two programs specified a policy to screen donors with anemia.

Thirty-four percent of centers (46/135) reported actually screening prospective donors for sickle trait in practice (question 2). Of centers that screened in practice, 19 reported screening only those of suspected African heritage. Six centers specified screening those of suspected African, Mediterranean or Indian subcontinent heritage.

One hundred five centers responded to question 3 about excluding donors with sickle trait. Eighteen percent (19/105) of centers reported that they would always exclude donors with sickle trait, nineteen percent (20/105) reported that they would exclude donors with sickle trait most of the time, forty-seven percent (49/105) reported that they would exclude donors with sickle trait rarely, and sixteen percent (17/105) reported that they would not exclude donors with sickle trait. These results are presented in Fig. 2.

Ninety-two programs reported performing <50 live donor transplants per year, 33 programs reported performing 50–100 live donor transplants per year, and six programs reported performing >100 per year. Six programs did not respond.

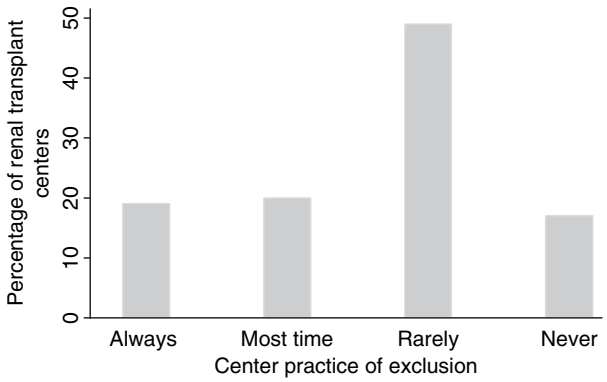

Figure 2 Variation in center practice toward excluding live kidney donors with sickle trait (n = 105).

High volume centers were more likely to screen donors for sickle trait in practice (Fisher's exact, $P = 0.03$). We found no association between center volume and screening policy (Fisher's exact, $P = 0.51$), or between center volume and exclusion of donors on the basis of sickle trait (Fisher's exact, $P = 0.25$).

Discussion

Although sickle trait is not rare, our results demonstrate that only a minority of transplant centers have a policy regarding screening live donors for sickle trait or screen for sickle trait in practice. Wide variation is evident in center practice regarding exclusion of donors on the basis of sickle trait.

Among centers that did describe a policy of screening donors for sickle trait, most reported that their policy was to screen donors who reported a family history of sickle disease. Only two reported that sickle trait screening would be prompted, if a patient were anemic. Thus, these centers seem to have an approach of 'selected screening.' One potential problem with adopting a 'selected screening' approach to sickle trait, however, is that many donors may not be aware or may not report that they carry the gene for Hemoglobin S. Alternatively, an expanded 'selected screening' approach might include screening racial or ethnic groups in which sickle trait has a higher prevalence. Interestingly, centers were less likely to test routinely potential donors of Mediterranean or Indian subcontinent heritage than potential African–American donors. This finding may reflect a lack of awareness that sickle trait is common in Mediterranean and Indian patient populations.

Our results show wide variation in centers' approach to excluding donors with sickle trait. Thirty-seven percent (39/105) of centers reported that they would exclude a potential donor with sickle trait always or most of the

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time, while sixty-three percent (66/105) would exclude such donors rarely or never. This variation probably reflects the paucity of studies about long-term effects of sickle trait in a nephrectomized patient. These differences in approach have important implications for clinical practice. If sickle trait does not increase the long-term risk of renal disease postnephrectomy, then centers that exclude donors on this basis may lose interested donors. On the other hand, if nephrectomy is not benign for donors with sickle trait, nephrectomy may put these donors at risk.

Our study showed that high volume centers (>100 live donor transplants) were more likely to screen donors for sickle trait in practice. It may be that centers that evaluate a larger number of live donors see more donors with isolated medical abnormalities. Notably, however, we found no consistent relationship between center volume and exclusion of live donors. Thus, high volume centers may be more likely to screen for sickle trait among donors, but their approach may simply be to educate these donors about their diagnosis rather than to exclude them from donation.

Potential limitations of our study include response bias. Approximately fifty-four percent (137/252) of the total transplant centers on the UNOS list responded to the questionnaire. Respondents, however, may differ from nonrespondents in unknown ways. Another limitation of our study is that we were unable to confirm whether responses were accurate. However, our questionnaires were addressed to transplant center directors, who would be expected to have familiarity with center policies and practices regarding live donors.

In summary, our study finds that only a minority of US transplant centers have a policy or practice to screen for sickle trait. Center practices about excluding potential donors with sickle trait also varied widely. Studies of renal outcomes in nephrectomized patients with sickle trait should be performed to clarify whether sickle trait poses a clinically important risk to donors. In the interim, transplant physicians must use individual judgment in putting this isolated medical abnormality in context when they discuss the potential risks of kidney donation with donors.

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Authorship

Designed study: PPR, CCM; Data collection: PPR, ACH; Analysis: PPR; Wrote the paper: PPR, CCM, ACH.

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References

1. Israni AK, Halpern SD, Zink S, Sidhwani SA, Caplan A. Incentive models to increase living kidney donation: encouraging without coercing. *Am J Transplant* 2005; **5**: 15.
2. Reese P, Caplan A, Kesselheim A, Bloom R. Creating a medical, ethical and legal framework for complex living kidney donors. *Clin J Am Soc Nephrol* 2006; **1**: 1148.
3. Steiner RW. Risk appreciation for living kidney donors: another new subspecialty? *Am J Transplant* 2004; **4**: 694.
4. Davis CL. Evaluation of the living kidney donor: current perspectives. *Am J Kidney Dis* 2004; **43**: 508.
5. Ataga KI, Orringer EP. Renal abnormalities in sickle cell disease. *Am J Hematol* 2000; **63**: 205.
6. Delmonico F. A report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; **6**(Suppl.): S53.
7. British Transplantation Society. *United Kingdom Guidelines for Living Donor Kidney Transplantation (7.0 Donor Evaluation)*. 2005. Available from: http://www.bts.org.uk/Forms/Guidelines_complete_Oct05.pdf [cited 10/9/2007].
8. Consensus conference. Newborn screening for sickle cell disease and other hemoglobinopathies. *JAMA* 1987; **258**: 1205.
9. Bruno D, Wigfall DR, Zimmerman SA, Rosoff PM, Wiener JS. Genitourinary complications of sickle cell disease. *J Urol* 2001; **166**: 803.
10. Trehan AWJ, Lane B, Foley R, *et al.* End-stage renal disease in Indo-Asians in the North-West of England. *QJM* 2003; **96**: 499.
11. Koppes GM, Daly JJ, Coltman CA, Butkus DE. Exertion-induced rhabdomyolysis with acute renal failure and disseminated intravascular coagulation in sickle cell trait. *Am J Med* 1977; **63**: 313.
12. Gupta AK, Kirchner KA, Nicholson R, *et al.* Effects of alpha-thalassemia and sickle polymerization tendency on the urine-concentrating defect of individuals with sickle cell trait. *J Clin Invest* 1991; **88**: 1963.
13. Noguera-Irizarry WG, Hibshoosh H, Papadopoulos KP. Renal medullary carcinoma: case report and review of the literature. *Am J Clin Oncol* 2003; **26**: 489.

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